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CASE REPORT

Desmopressin-Induced Severe Hyponatremia with Central Pontine Myelinolysis: A Case Report

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Abstract Desmopressin, a synthetic vasopressin analog, is used to treat central diabetes insipidus, hemostatic disorders such as von Willebrand's disease, and nocturnal enuresis. We present the case of a 69-year-old man who developed severe hyponatremia during treatment with intranasal desmopressin at 10 μg twice daily for chronic polyuria and nocturia thought to be due to central diabetes insipidus. After 5 months of therapy, the patient noticed progressive fatigue, anorexia, dizziness, weakness, lightheadedness, decreased concentration, and new-onset falls. At 6 months of therapy, the patient was brought to the emergency department for altered mental status and was found to be severely hyponatremic with a serum sodium level of 96 mmol/L, down from a value of 134 mmol/L at the initiation of therapy. The intranasal desmopressin was discontinued and the patient was admitted to the intensive care unit where the hyponatremia was slowly corrected over the next week to 132 mmol/L, never increasing by more than 8 mmol/L a day, with careful fluid management. This included infusion of over 11 L of 5% dextrose to account for a high urine output, which peaked at 7.4 L in 1 day. However, while the recommended rate for sodium correction was followed, the patient's magnetic resonance imaging of the brain obtained after discharge displayed evidence of central pontine myelinolysis. Despite this finding, the patient eventually returned to his baseline mental status with no permanent neurologic deficits.

Key Points

Desmopressin, a synthetic vasopressin analog used to treat central diabetes insipidus and nocturnal enuresis, can induce a severe hyponatremia if administered without proper monitoring of serum electrolytes.

The discontinuation of desmopressin can lead to severe diuresis and a rapid rise in serum sodium levels without careful management of fluid status in an intensive care setting.

Central pontine myelinolysis secondary to rapid sodium correction can still be seen in patients who have their serum sodium levels normalized at the suggested appropriate rate.

Introduction

Desmopressin, a synthetic vasopressin analog, is used to treat central diabetes insipidus, hemostatic disorders such as von Willebrand's disease, and nocturnal enuresis [1–10]. Desmopressin works on hemostasis by stimulating the release of endogenous von Willebrand factor into the plasma and on diabetes insipidus by increasing the absorption of free water in the collecting tubules of the renal nephron [11, 12]. However, desmopressin-induced

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inappropriate antidiuretic hormone levels with subsequent water intoxication have been associated with severe hypervolemic hyponatremia and seizures, especially with intranasal formulations and administration at extremes of age [7–9, 13–30]. Osmotic myelinolysis in conjunction with desmopressin is a rare occurrence, but can occur as this case report demonstrates [31–35].

Case Report

The patient is a 69-year-old man with hypertension on amlodipine, hypogonadism on testosterone therapy, and chronic polyuria thought to be due to central diabetes insipidus on intranasal desmopressin at 10 μg twice daily who presented to the emergency department from his primary care physician's office 6 months after initiation of desmopressin with 1 month of progressive fatigue, anorexia, dizziness, weakness, and gait instability that worsened in the week prior to presentation. He denied any fevers, headaches, neck pain, chest pain, nausea, vomiting, diarrhea, dark stools, or leg swelling, but did note increased thirst with up to 1 gallon of water intake daily for several weeks. His past medical history also included hyperlipidemia, obesity with mild obstructive sleep apnea, gastroesophageal reflux disease with esophagogastric fundoplication, and benign prostatic hyperplasia with green light photovaporization.

On examination in the emergency department, the patient had normal vital signs and was alert but was very lethargic and had an unstable gait. A non-contrast computed tomography scan of the head on the day of admission demonstrated no acute intracranial processes. However, a basic metabolic panel revealed a sodium level of 96 mmol/L, which was down from 125 mmol/L 2.5 months prior to presentation, and down from a value of 134 mmol/L at the initiation of desmopressin 6 months prior. Additionally, the patient's urine sodium level was 37 mmol/L and he had normal thyroid-stimulating hormone and cortisol levels. Given the patient's profound hyponatremia with changes in mental status, hypertonic saline was administered and admission to the medical intensive care unit was initiated.

In the medical intensive care unit, the patient was placed on an 800-mL/day fluid restriction, taken off the hypertonic saline, and placed on a dextrose infusion to match urine output. The patient required infusion of over 11 L of 5% dextrose (Fig. 1) to match a high urine output, which peaked at 7.4 L on the second day of admission and then tapered down to 1.5 L by hospital day 5 (Fig. 2). Over the course of 4 days in the medical intensive care unit, the patient's sodium levels steadily increased to 125 mmol/L (never rising above 8 mmol/L in a day) with improvement in his mental status and symptoms (Fig. 3). The patient was

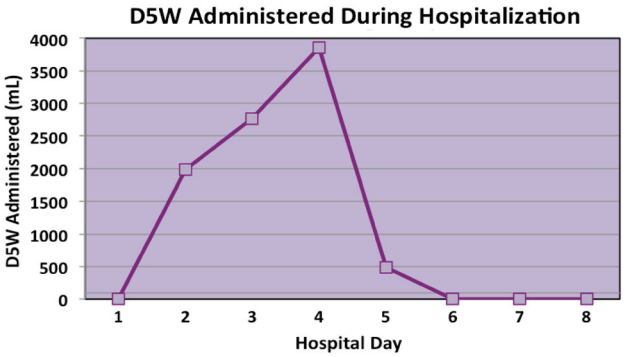

Fig. 1 Dextrose 5% water (D5W) administered during hospitalization

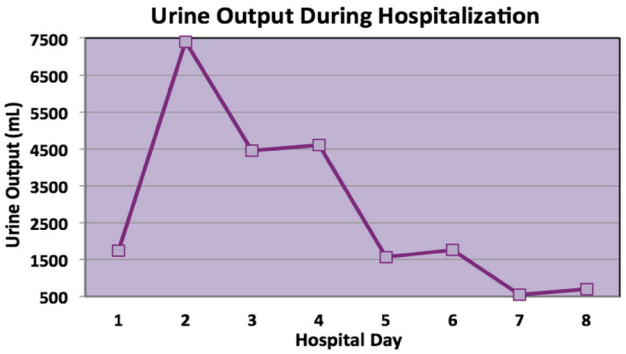

Fig. 2 Urine output during hospitalization

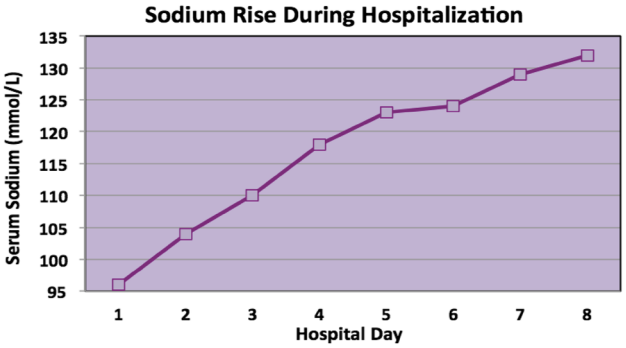

Fig. 3 Serum sodium level during hospitalization

then transferred to the medicine unit with stabilization of his serum sodium levels between 130 and 132 mmol/L on repeated checks prior to discharge home.

At discharge, the patient was instructed to discontinue his desmopressin. Repeat sodium levels on outpatient follow-up remained stable between 136 and 139 mmol/L. However, as seen in Fig. 4, comparing a magnetic resonance imaging study of the brain obtained on day 3 of admission to one obtained on day 25 after admission revealed a slight irregular T2 hyperintensity in the central part of the pons, likely consistent with central pontine osmotic myelinolysis. Despite this finding, the patient

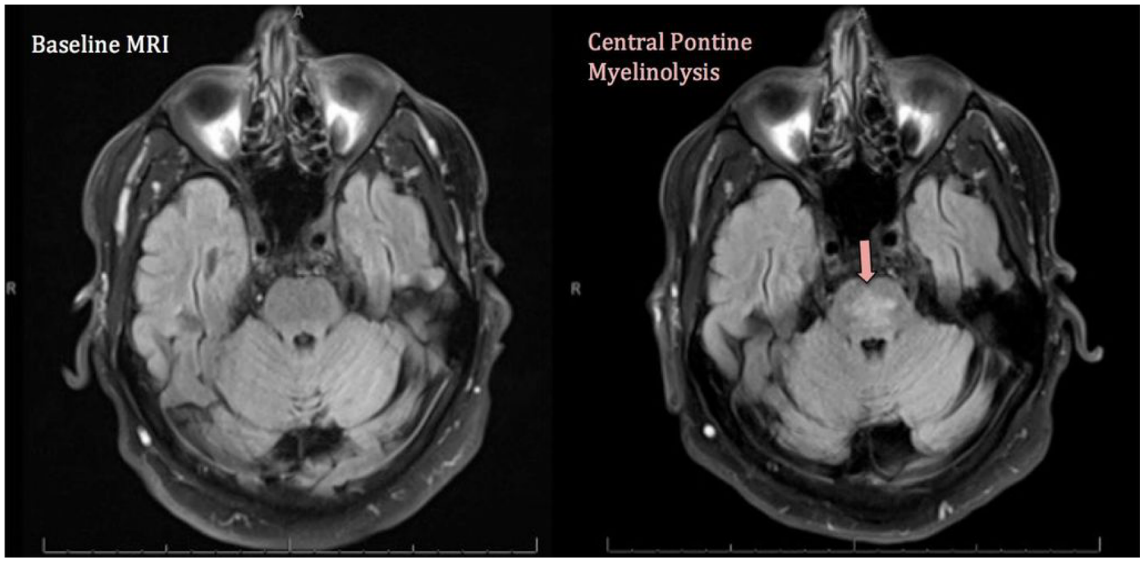

Fig. 4 Magnetic resonance imaging (MRI) with evidence of central pontine myelinolysis. Baseline is on hospital day 3. Central pontine myelinolysis is seen on day 25 after admission

eventually returned to his baseline mental status with no permanent neurologic deficits observed at the 2-year follow-up. The central diabetes insipidus continued for several months and then went into remission.

Discussion

Desmopressin-induced hyponatremia can have severe neurologic consequences for patients. Although it is an effective medication for hemostatic disorders, central diabetes insipidus, and nocturnal enuresis, it can be harmful without adequate monitoring of electrolytes and fluid intake or appropriate patient education on side effects [9, 13, 14, 17, 22, 28]. In this case, our patient was started on intranasal desmopressin for nocturnal enuresis with an adequate response but with an inadequate follow-up of his serum electrolytes until the patient presented to the emergency department with severe hyponatremia and mental status changes. The patient had a steady decline in his serum sodium level from 134 to 96 mmol/L over the course of 6 months. Then, on presentation to the hospital, there was an abrupt discontinuation of desmopressin, which in turn led to a large diuresis during the initial days of hospitalization. This massive shift in body fluids required careful monitoring in an intensive care setting to ensure adequate repletion of urinary fluid losses to maintain the body's fluid balance as well as to ensure a controlled increase in the body's serum sodium level.

In this case, although the suggested rate of serum sodium rise of 8-mmol/L/day was followed, the patient still experienced the consequence of central pontine myelinolysis as documented by magnetic resonance imaging changes at the level of the pons seen on imaging 25 days after admission that was not as evident on a baseline magnetic resonance imaging obtained on day 3 of hospitalization. It is possible that in this patient's case even the 8-mmol/L/day recommendation may have been too rapid a correction given the patient's serum sodium levels declined slowly over the course of 6 months. In such a case, an even slower rate of increase to correct the serum sodium level may be warranted. An additional approach to ensure an appropriate rate of correction would entail tapering the patient off the intranasal desmopressin over time with decreasing frequency and dosage instead of suddenly stopping it at presentation in the emergency department. Lastly, despite evidence of central pontine myelinolysis by imaging, it is possible to recover without any permanent focal neurologic deficits, as evidenced by our patient's return to his baseline neurologic function that persisted at 2 years' post-hospitalization.

Conclusion

Desmopressin can induce significant hyponatremia leading to very severe neurologic consequences for patients. The management can be complex, as discontinuation of desmopressin can lead to profuse diuresis and a rapid rise in sodium levels as a result of suppressed antidiuretic hormone levels. This requires very careful monitoring of a patient's fluid input and output to match the diuresis with appropriate free water replacement. Furthermore, the normalization of the hyponatremia can be complicated by

central pontine myelinolysis even when the sodium is carefully titrated. Although it is an effective medication for central diabetes insipidus, desmopressin can be harmful with inadequate monitoring of patient fluid status and electrolytes.

Compliance with Ethical Standards

Funding No financial support was received for the preparation of this case report.

Conflicts of Interest Tanzib Hossain, Marya Ghazipura, Vineet Reddy, Pedro J. Rivera, and Vikramjit Mukherjee have no conflicts of interest directly relevant to the content of this case report.

Consent to Participate Written informed consent was obtained from the patient for publication of this case report with accompanying images for educational purposes and can be requested for review from the corresponding author.

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